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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,327	02/21/2002	Tim Hui-Ming Huang	40629-2	3584

22504 7590 12/22/2005

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EXAMINER

GOLDBERG, JEANINE ANNE

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 12/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/081,327

Applicant(s)

HUANG, TIM HUI-MING

Examiner

Jeanine A. Goldberg

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 September 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This action is in response to the papers filed September 21, 2005. Currently, claims 1-17 are pending.
2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is made FINAL.
3. Any objections and rejections not reiterated below are hereby withdrawn.

Maintained Rejections

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-16, 21 of U.S. Patent No. 6,605,432.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably

distinct from the reference claim(s) because the examined claim is either anticipated by or would have been obvious over, the reference claim(s). See e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentable distinct from each other because Claims 1-17 of the instant application has been amended to require all the limitations of Claims 1-16, 21 of U.S. Patent No. 6,605,432 with the exception of "lacks a CpG dinucleotide sequence". However, Claim 12 is directed to particular examples which lack a CpG dinucleotide, as set forth in the specification, page 27. Furthermore the specification states on page 27, that is it preferred that the restriction enzyme used is an enzyme which has a recognition sequence in regions other than the CpG dinucleotide rich regions of the nucleotide sequence. Thus, Claim 1-16, 21 of 6,605,432 obvious in view of Claim 1-17. Here, claim 1-16, 21 of U.S. Patent No. 6,605,432 recites a method for detecting the presence or absence of methylation of CpG dinucleotide rich regions of nucleic acid sequences by contacting with an enzyme, ligating a linker, digesting with an enzyme, amplifying, labeling, contacting with an array and determining the presence of labeled amplicons.

Allowable Subject Matter

5. The claims have been amended to require particular enzymes which are not methylation-sensitive and lacks a CpG dinucleotide sequence in its recognition motif.

Page 27, at least of the specification, states that restriction enzyme digests the portions of the nucleotide sequence not containing CpG dinucleotides (lines 20-25).

The closest prior art neither teaches nor suggests the claimed invention. Duffy (US Pat. 5,871,917, February 16, 1999) teaches detection of methylated nucleic acids using methylation sensitive enzymes to cleave genomic DNA; placing linkers on the fragments and amplifying. Duffy differs from the claimed invention in that Duffy digests with a methylation sensitive enzyme followed by ligation of linkers. The linkers of the instant invention are not ligated to ends cut by a methylation sensitive enzyme. Thus, the fragments generated by the two methods differ in the products generated to be amplified.

Donini et al (Genome, Vol. 40, pages 521-526, 1997) teaches an AFLP fingerprinting method to reveal differences between template DNA from various plants. Donini teaches using DNA, fragmenting the nucleic acid and amplifying the nucleic acid. However, Donini amplifies all fragments. Donini fails to teach to cleaving of non-methylated and amplification of only the methylated fragments.

Zabeau et al (US Pat. 6,045,994, filed January 1994) teaches a method using two restriction enzymes for selective restriction fragment amplification. Zabeau teaches using both PstI (methylation sensitive) and MseI (methylation insensitive) in combination; ligating MseI and PstI adapters to the fragments; separating; amplifying and analyzing (Example 2). The method of Zabeau differs from the instant method because Zabeau creates three types of fragments from the two enzymes (i.e. PstI-PstI; PstI-MseI; MseI-MseI). Moreover, Zabeau teaches capturing the biotinylated fragments

from non-biotinylated fragments to amplify using PstI primers. The instant invention contains only fragments which ends are linked to a methylation insensitive adapter and contain an internal methylated CpG island.

Finally, Vuylsteke et al (US Pat. 6,300,071, filed July 28, 1999) teaches method of detecting nucleic acid methylation using AFLP. It is noted that the provisional applications in the instant application, which support the claimed invention, were filed in February 1999, therefore, Vuylsteke is not considered prior art. However, Vuylsteke teaches in Figure 1, panel B a method of digesting DNA using MseI (a methylation insensitive enzyme); amplification; digestion with PstI a methylation sensitive enzyme and finally amplification.

Conclusion

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

Art Unit: 1634

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272- 0745.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.



Jeanine Goldberg

Primary Examiner

December 19, 2005